REMARKS

Rejection Under 35 U.S.C. 103(a)

According to the Advisory Action, the Request for Reconsideration does not place the application in condition for allowance. Although the Examiner acknowledges that neither Engelke et al. nor Livache et al. teach the claimed oligonucleotide primers, the Examiner maintains the obviousness rejection of claims 1-9, 17, 19-23 and 30-32.

The Examiner relies on Engelke et al. for the suggestion that "it was common sense in the art that oligonucleotide primers are used to synthesize a desired target sequence . . . wherein the oligonucleotide primers are used in PCR-based amplification methods." The Examiner then relies on Livache et al. for disclosure of "a PCR-based amplification method comprising primers complementary to the 5' promoter sequence." According to the Examiner, Livache et al. suggest that "each oligonucleotide primer comprise a complementary sequence to the 5' end or a 3' end promoter sequence when a single promoter sequence, instead of two promoters, is to be used for transcribing an RNA duplex."

The Examiner concludes that "one of ordinary skill in the art would have reasonably determined necessary PCR reaction reagents for producing a U6 promoter-containing double-stranded siRNA expression cassette" including the claimed primers. In making this conclusion, the Examiner appears to also assume disclosure of a primer comprising a complementary sequence to the 3' end of the U6 promoter that also comprises a sequence complementary to a sequence encoding either a sense or antisense sequence of a siRNA molecule "because the two strands of the siRNA duplex to be transcribed is operably linked to 3' end of the U6 promoter sequence."

The Examiner further concludes that the claimed invention as a whole would have been *prima facie* obvious at the time of filing, and relies on the following points as the basis for this conclusion:

1) the structure of an expression cassette comprising a mammalian promoter (e.g. U6) operably linked to a double-stranded siRNA sequence was known in the art (Engelke et al., Figure 4, paragraph 0014);

2) the practical utility of the siRNA expression cassette for long-term expression siRNA in an animal cell with reduced expenses was known in the art (Engelke et al.);

3) PCR amplification method for synthesizing expression cassettes was known to be more rapid compared to the restriction-enzyme-based cloning method of Engelke et al.; and

4) the method of PCR-based synthesis/amplification of a promoter-containing target sequence was known in the art (Livache et al.) and it was common sense in the art that oligonucleotide primers are used to synthesize a desired target sequence

Applicants respectfully disagree. First, the Examiner has misinterpreted Livache et al. as teaching or suggesting oligonucleotide primers comprising a complementary sequence to the 5' end or a 3' end promoter sequence. The relevant cited portion of Livache states the following:

> The third method consists of integrating primers carrying in 5' promoter sequences of at least one RNA polymerase in the DNA to be transcribed by an amplification process such as PCR . . .

Col. 3, lines 56-59 (emphasis added). Livache et al. in actuality teaches that the promoter sequences are integrated at the 5' end of the primer. This is logical since the target sequence is synthesized from the 3' end of the primer. As explained in the Request for Reconsideration, Applicants maintain that Livache et al.'s primers comprise/contain/integrate the full promoter sequence at the 5' end, rather than flank a target promoter sequence. Also, Livache et al.'s invention is a "process for preparing double-stranded RNA" wherein "simultaneous transcription is carried out of the two complementary strands of a DNA sequence." Col. 2, lines 23-26. Livache et al. cannot be interpreted as teaching or suggesting primers that are complementary to the 5' end or 3' end of a promoter sequence (and amplification of a promoter sequence) because such an interpretation would not permit simultaneous transcription of RNA. If the promoter sequence is the target sequence for PCR amplification and primers complementary to the 5' end and 3' end are used, there would not be any non-promoter DNA sequence to simultaneously transcribe. Thus, Livache et al. does not – and in fact, cannot - teach or suggest primers that comprise a complementary sequence to the 5' end or 3' end of a promoter sequence.

Second, the Examiner's reliance on the disclosures of Engelke et al. and Livache et al. and "common sense in the art" (points 1-4 described above) do not resolve the deficiencies identified in our Request for Reconsideration. In particular, neither reference discloses a primer that is complementary to a promoter sequence and comprises a sequence which is complementary to a sequence encoding either a sense or antisense strand of a siRNA molecule. Engelke et al.'s disclosure of an expression cassette comprising a mammalian promoter linked to a double stranded siRNA sequence - in combination with knowledge in the art regarding the speed of the PCR amplification method and use of PCR to amplify a target sequence - falls short of describing the presently claimed primers. Common sense would only lead one skilled in the art to start with a DNA template that comprises a promoter sequence and a sequence encoding either a sense or antisense strand of a siRNA molecule and to use primers that flank both of these target sequences for amplification. PCR *amplification* of the Engelke et al. expression cassettes does not require primers with the claimed features. Thus, the Examiner has not established a *prima facie* case of obviousness.

With respect to claims 30-32, Applicants maintain that neither Noonberg et al. nor Dietz cures the deficiencies of the combined teachings of Engelke et al. and Livache et al. Neither of these references disclose PCR amplification of a promoter sequence in which a first primer is complementary to the 5' end of the mammalian promoter sequence and a second primer is complementary to the 3' end of the mammalian promoter sequence and comprises a sequence which is complementary to a sequence encoding either a sense or antisense strand of a siRNA molecule.

In view of the above remarks, Applicants submit that Engelke et al., Livache et al., Noonberg et al. and Dietz do not teach or suggest all of the elements of the claimed subject matter and thus do not render the claimed subject matter obvious. Also, Applicants maintain that neither the references nor common sense of one of ordinary skill in the art provide(s) proper motivation to combine the teachings of the prior art.

Conclusion

In view of the above remarks, Applicants believe that the pending claims satisfy the provisions of the patent statutes and are patentable over the cited prior art. Reconsideration of the application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

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